PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P2724WO	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/EP2004/006530	International filing date *(day/month/year)* 17.06.2004	Priority date *(day/month/year)* 24.06.2003
International Patent Classification (IPC) or national classification and IPC A61F2/30		
Applicant STIFTUNG, ROBERT MATHYS		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 7 sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
17.02.2005	18.07.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Arjona Lopez, G Telephone No. +49 89 2399-2546

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/006530

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-24	as originally filed
Claims, Numbers	
1-33	received on 17.05.2005 with letter of 17.05.2005
Drawings, Sheets	
1/1	as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 32,33

because:

☒ the said international application, or the said claims Nos. 32,33 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees, the applicant has:
   - ☐ restricted the claims.
   - ☐ paid additional fees.
   - ☐ paid additional fees under protest.
   - ☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-30 .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-30
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-29
	No:	Claims	30
Industrial applicability (IA)	Yes:	Claims	1-30
	No:	Claims	

2. Citations and explanations (Rule 70.7):

   see separate sheet

The following documents (D) are referred hereto; the numbering will be adhered to in the rest of the procedure:

D1: WO-A-98/53768
D2: US-A-2001/0039455
D3: EP-A-1 277 450

Re Item III.

1. As to independent claim 31, the subject-matter of the latter is not linked through an inventive concept to claims 1-30 (Rules 13.1 and 13.2 PCT, see also Re Item IV below); and

2. As to claims 32-33, the subject-matter of these claims refers to a method for treatment of the human or animal body by surgery (Rule 39.1(iv) PCT), for the following reason:

2.1 Claims 32-33 define "a use of the device according to at least one of the preceding claims **for implantation**... in humans and animals". Thus, the subject-matter of claims 32-33 refers to a method of treatment of the human body by surgery in the sense of Article 52(4) EPC and it is regarded as not being patentable. Hence those claims should be deleted from the application. Reference of such a method as being part of the invention should also be deleted from the description.

Re Item IV.

The separate inventions of inventions are:

I-Claims 1-30: A prosthetic device for repairing or replacing cartilage comprising at least one layer comprising at least partially oriented fibres, a base component to anchor said layer of fibres in subchondral environment and a stabilization area between said at least one layer comprising fibres and said base component; and

II-Claim 31: A prosthetic device for repairing or replacing cartilage comprising at least one

layer comprising fibres, a base component to anchor said layer of fibres in subchondral environment and a cell barrier layer between said at least one layer comprising fibres and said base component.

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

The common concept linking together the subject-matter of independent claims 1,30 and 31 is a prosthetic device for repairing or replacing cartilage comprising at least one layer comprising fibres, a base component to anchor said layer of fibres in subchondral environment and an area in between. Document D2 discloses a three layer cartilage plug (cf. figure 1; paragraph 0109), from which the above common concept linking together the subject-matter of claims 1,30,31 differs in that the at least one layer comprises fibres. Nevertheless no inventive idea can be seen in the latter feature, since this is a matter of normal design for reinforcing the polymeric implant material, see for example documents D3 (cf. column 4, lines 50,53-55) and D1 (cf. page 1, lines 22-24; page 2, lines 14-18).

Re Item V.

1. Claims 1 and 30 have been drafted as separate independent claims. Nevertheless, as explained below, the subject-matter of claim 1 is contained in claim 30 and therefore claim 1 is dependent on independent claim 31. The orientation defined in claim 1 "parallel to the insertion axis of the device" is equivalent to the definition in claim 30 of a direction "perpendicular to a top surface of the base component facing the fibres", see the description page 5, lines 17-24. Therefore, claim 1 defines all the features of independent claim 30 plus the feature that the fibres form a brush-like structure.

2. The present application does not meet the criteria of Article 33(1) PCT, because the subject matter of independent claim 30 does not involve an inventive step in the sense of Article 33(3)PCT. Document D1 (cf. page 2, line 14-page 3, line 6, lines 20-29; page 7, lines 8-10; page 15, lines 17-26; claim 6) discloses a prosthetic device for repairing or replacing cartilage or cartilage like tissue comprising at least one layer

comprising at least partially oriented fibres, a base component to anchor said at least one layer of fibres in subchondral environment (cf. specially page 7, lines 8-10; page 15, lines 17-26; claim 6), whereby the fibres are aligned perpendicular to the surface of the cartilage (cf. specially page 2, lines 22-28), i.e. perpendicular to the surface of the base component (note that document D1 cites U.S. Patent No. 5,607,474 as an example of a multiphase implant and this document discloses a cylindrical cartilage plug). The subject-matter of claim 30 differs from this know device in that between the layer comprising fibres and the base component there is a stabilization area.

2.1 The problem to be solved by the present invention may therefore be regarded as to provide the implant with more stability.

2.2 The solution proposed in claim 30 of the present application cannot be considered as involving an inventive step, since the feature of providing a stabilization zone between the layer comprising fibres and the base layer is described in document D2 (cf. figure 1; paragraphs 0109 and 0111) as providing the same advantages as in the present application. The skilled person would therefore regard it as a normal option to include this feature in the prosthetic device described in document D1 in order to solve the problem posed.

3. As to dependent claim 1, the subject-matter of claim 1 differs from the known prosthetic device of document D1 in that between the layer comprising fibres and the base component there is a stabilization area and that said fibres form a brush-like structure. The latter feature helps to mimic the cartilage-like tissues and provides for mechanical stability. At the same time a basis for the ingrowth of articular chondrocytes is provided resulting in a rapid cartilage growth, thus assuring a long term cartilage replacement.

4. The claims 2-29 are dependent on claim 1 and, thus, also meet the requirements of the PCT with respect to novelty and inventive step.

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Amended Claims

1. A prosthetic device for repairing or replacing cartilage or cartilage like-tissue (1) comprising
   - at least one layer comprising at least partially oriented fibers (2),
   - a base component (4) to anchor said at least one layer of fibers (2) in subchondral environment and
   - a stabilization area (3) provided between said at least one layer comprising fibers (2) and said base component (4),

   wherein said fibers (2) are aligned essentially in parallel to the insertion axis of the prosthetic device and form a brush-like structure.

2. The device according to claim 1, wherein said fibers (2) are aligned to more than 50, preferably more than 90 %.

3. The device according to claim 1 or 2, wherein the fiber material (2) includes a mineral material, synthetic polymers or molecules, natural polymers or molecules, biotechnologically derived polymers

or molecules, biomacromolecules, or any combination thereof.

4. The device according to claim 3, wherein the fiber diameter is in a range of 50 nm to 1 mm.

5. The device according to claim 4, wherein said fiber diameter is in a range of 1 µm to 250 µm.

6. The device according to any of claims 3 to 5, wherein the fibers (2) have a liquid absorbing capacity in a range of 0,1 to 99,9 %.

7. The device according to claim 6, wherein said liquid absorbing capacity is in a range of 20,0 to 99,0 %.

8. The device according to claim 6 or 7, wherein the liquid is an aqueous solution and/or body fluids.

9. The device according to at least one of claims 1 to 8, wherein the base component (4) comprises a material used as a bone substitute.

10. The device according to claim 9, wherein said bone substitute is a material as defined in claim 3.

11. The device according to claim 9, wherein said material is a synthetic ceramic containing at least one of the following components: calcium phosphate, calcium sulfate, calium carbonate, or any mixture thereof.

12. The device according to claim 11, wherein said calciumphosphate containing at least one of the following components: di-calciumphosphatedihydrate ($CaHPO_4x2H_2O$), dicalciumphosphate ($CaHPO_4$), alpha-tricalciumphosphate (alpha-$Ca_3(PO_4)_2$), beta-tricalciumphosphate (beta-$Ca_3(PO_4)_2$), calcium deficient hydroxylapatite ($Ca_9(PO_4)_5(HPO_4)OH$), hydroxylapatite ($Ca_{10}(PO_4)_6OH_2$), carbonated apatite ($Ca_{10}(PO_4)_3(CO3)_3)(OH)_2$), fluorapatite ($Ca_{10}(PO_4)_6(F,OH)_2$), chlorapatite ($Ca_{10}(PO_4)_6(Cl,OH)_2$), whitlockite ($(Ca,Mg)_3(PO_4)_2$), tetracalciumphosphate ($Ca_4(PO_4)_2O$), oxyapatite ($Ca_{10}(PO_4)_6O$), beta-calciumpyrophosphate (beta-$Ca_2(P_2O_7)$), alpha-calciumpyrophosphate, gama-calcium-pyrophosphate, octacalciumphosphate ($Ca_8H_2(PO_4)_6x5H_2O$).

13. The device according to claim 9, wherein said material is a synthetic ceramic containing

metallic, semimetallic ions, and/or non-metallic ions, preferably magnesium, silicon, sodium, potassium, and/or lithium.

14. The device according to any of the claims 9-11b wherein the material is a composite material comprising at least a polymer component and a mineral phase.

15. The device according to any of claims 9 to 14, wherein the bone substitute material is highly porous with interconnecting pores.

16. The device according to any of claims 9 to 15, wherein the shape of the base component (4) is round cylindrical or conical.

17. The device according to claim 16, wherein the diameter of the base component (4) ranges between 2 and 30 mm, with a height being 1 to 30 mm.

18. The device according to claim 16, wherein the diameter of the base component (4) ranges between 4 and 20 mm, with a preferred height being between 1 to 6 mm.

19. The device according to at least one of claims 1 to 18 wherein said stabilization area (3) is a zone comprising at least one layer.

20. The device according to claim 19, wherein said zone has a thickness of 1 nm to 1 mm.

21. The device according to claim 19 or 20, wherein said zone is porous.

22. The device according to any of claims 19 to 21, wherein the layer system is composed of a chemical substance.

23. The device according to at least one of preceding claims, further comprising at least one externally added component.

24. The device according to claim 23, wherein said components are cells of different origin.

25. The device according to claim 24, wherein said cells are autologous cells, allogenous cells, xenogenous cells, transfected cells and/or genetically engineered cells.

26. The device according to claim 23, 24 or 25, wherein chondrocytes, chondral progenitor cells, pluripotent cells, tutipotent cells or combinations thereof are present throughout the fiber layer(s) (2).

27. The device according to claim 23, 24 or 25, wherein osteoplasts, osteo progenitor cells, pluripotent cells, tutipotent cells or combinations thereof are present throughout the base component (4).

28. The device according to claim 23, 24 or 25, wherein blood or any fraction thereof is present throughout the base component (4).

29. The device according to claim 23, wherein pharmaceutical compounds are contained.

30. A prosthetic device for repairing or replacing cartilage or cartilage like-tissue (1) comprising
- at least one layer comprising at least partially oriented fibers (2),
- a base component (4) to anchor said at least one layer of fibers (2) in subchondral environment and
- a stabilization area (3) provided between said at least one layer comprising fibers (2) and said base component (4),

wherein said fibers (2) are aligned essentially perpendicularly to a top surface of the base component facing the fibers.

31. A prosthetic device for repairing or replacing cartilage or cartilage like-tissue (1) comprising
- at least one layer comprising fibers (2),
- a base component (4) to anchor said at least one layer of fibers (2) in subchondral environment and
- a cell barrier layer provided between said at least one layer comprising fibers (2) and said base component (4).

32. A use of the device according to at least one of the preceding claims for implantation in articulating joints in humans and animals.

33. The use according to claim 32 for regeneration of articulator cartilagenous tissue.